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DEPARTMENT OF THE ARMY
Fort Detrick
Frederick, Maryland

STUDY OF THE EFFECTS OF LYOPHILIZATION ON BILIARY CATATONIA

[Following is a translation of an article
by H. Baruk, M. Asfar, and A. Vittoz in
the French-language journal Comptes Rendus
Soc. Biol., (Proceedings of the Biological
Society), Vol 157, Paris, pages 110-112.] 1163

In previous studies with L. Camus one of us has shown, in the bile of certain sufferers from jaundice or schizophrenia, a toxic principle producing an experimental catatonia in animals, especially in the pigeon. ([Note]: H. Baruk and L. Camus, C. R. Soc. Biol., 1934, Vol. 116, page 403). He has emphasized the relationship of schizophrenia to certain jaundices. ([Note:] H. Baruk and R. Cornu, "Schizophrenia and Jaundice," Ann. Med. Psych., No 4, November 1934). It was shown that the cataleptizing toxic principle was distinct from the normal constituents of bile, that it persisted in biles completely decolorized after clarification by the salts of certain heavy metals, while this toxic principle was destroyed by a heat of 100 degrees [centigrade]. ([Note:] H. Baruk and L. Camus, Presse Medicale, 1949, page 1065). These facts were confirmed by various authors, particularly by Mall in Germany, who found in addition an analogous substance in certain epileptics ([Note:] G. Mall, "On the Toxicity of the Bile and Serum in Epileptics and Schizophrenics," Moreau Society of Tours, 29 November 1959. Annales Moreau de Tours, Vol. 1 (Presses Universitaires de France, 1962), page 349).

Subsequently one of us revealed a paralyzing principle in other cases. He thought at first that the production of these paralyses was largely due to an excess of bile acids. Afterwards, however, he wondered whether he was not dealing with a special neurotropic poison. Finally, in a third stage, he determined that the same toxic bile could produce in the

animal (when the poisoning was moderate) an experimental catatonia, while when the poisoning was more acute it produced paralyzes. This is what he has called psycho-organic periods. ([Note:] H. Baruk and L. Camus, C. R. Soc. Biol., 1934, Vol 84, No 4; H. Baruk and J. Launay, "The Law of Periods and Experimental Psychopharmacology in Monkeys," Second International Congress of the Neuropsychopharmacological Collegium, Basle, 1960, Vol 2 (1961)).

The identification of this catatonia producing toxic product has given rise to many research projects. One of us, with Claude and Olivier, had already insisted on the polypetidorachy and hepatic insufficiency in cataleptic sleep and catatonic stupor. ([Note:] H. Claude, H. Baruk, and H. R. Olivier, C. R. Soc. Biol., 1932, Vol 110, page 1275; H. Baruk, Richordeau and Asfar, Ann. Med. Psych., 1962, Vol 2, page 554). The researches of Launay, Perles and Cournut showed in these toxic biles the heightening of optical density, and the passing by dialysis of the toxic principle with the large molecules ([Note:] J. Launay, Perles and Cournut, Ann. Med. Psychol., 1962, Vol 2, page 99). The problem of the polypeptids in this field has come up lately in the American work on the P substance. ([Note:] B. Pernow, "Effect of Substance P on Smooth Muscle," in Polypeptides (Pergamon Press), Vol 4 of Symposium, March 1959, pages 171-194.) All the researchers agree in thinking that they are dealing with a fragile protein substance (Buscaino in Italy, Georgi at Basle, etc.).

It is with this purpose in mind that we submitted a series of toxic catatonia producing biles to lyophilization to see whether lyophilization would modify their toxic power.

The results of these investigations are set forth in the table.

Conclusions

The examination of this table using the bile of eight patients suffering from mental troubles shows:

1. That lyophilization in a general fashion clearly modified the pathogenic action of biles in animals. Certain biles producing catatonia before lyophilization lose this property after lyophilization. The same is true for the paralyzing and general toxic action, especially in cases 5 and 6 where the fresh bile caused paralysis and death of the animal before lyophilization while after lyophilization these same biles had no effect or else caused only a slight passing loss of initiative.

2. The same is true of the high optical density of toxic biles; this optical density also goes down after lyophilization.

3. These results favor the hypothesis that considers the biliary catatonia producing agent as a particularly fragile product. [Note:—Work carried out thanks to the help of the General Body of Delegates for Scientific and Technical Research (Committee for Neurophysiology and Pharmacology)].

(Laboratory for Experimental Psychopathology of the Practical School for Advanced Studies [Director: Mr. H. Baruk]).

| Before Lyophilization | | | | |
|---|--|--|--|---|
| Name | Bile A | | Bile B | |
| | Optical Density | Pigeon Test | Optical Density | Pigeon Test |
| 1. Roz (age 27) | | | BO°=0.08 BE=0.12 | Dead half an hr. later. |
| 2. Miss Fr. (age 35) Before treatment, depression with seri- ous mes- thesia | 18 Jun '62 BO°=0.06 BF=0.13 BE=0.12 | 18 Jun '62 a. Paralyzes b. Troubles in balance c. Falling to ground test+++ (catalepsy); 24 hrs later, disappearance of catalepsy. | BO°=0.21 BF=0.29 BE=0.28 | Sleep, no catalepsy. Died 24 hrs. later. |
| 3. Mrs. Fr. (age 37) After treat- ment (Sato principle) | 26 Jun '62 BO°=0.06 BF=0.13 BE=0.12 | 26 Jun '62 Normal Tests ne- gative Died 27 Jun | 26 Jun '62 BO°=0.15 BF=0.20 BE=0.20 | 26 Jun '62 Normal Tests ne- gative. 27 June: trembling 28 June: normal |
| 4. Mrs. Ok. (age 37) depression, alcoholism | 18 Jun '62 BO°=0.11 BF=0.09 BE=0.14 | 18 Jun '62 Slight trembling, sleep posi- tion. 24 hrs later, paralysis of feet. | 18 Jun '62 BO°=0.08 BF=0.09 BE=0.09 | 18 Jun '62 Sleep Then normal the follow- ing days. |

Continued.....

| After Lyophilization | | | |
|-----------------------|----------------------------------|--|---|
| | <u>Bile A</u> | <u>Bile B</u> | |
| | <u>Optical</u> <u>Density</u> | <u>Pigeon</u> <u>Test</u> | <u>Optical</u> <u>Density</u> <u>Pigeon</u> <u>Test</u> |
| 1. | | | 0.11 Normal behavior |
| ----- | | | |
| 2. 0.14 | | 16 July '62 a. normal ap- pearance b. No balance c. Falling to ground test negative d. No catalepsy | 0.17 16 July '62 Normal |
| ----- | | | |
| 3. | | | |
| ----- | | | |
| 4. 21 Jun '62 0.15 | | 21 Jun '62 Normal (cultures of bile negative) | 0.14 Normal |
| ----- | | | |

Continued.....

| Name | Before Lyophilization | | | |
|--|--|---|--|--|
| | Bile A | | Bile B | |
| | Optical Density | Pigeon Test | Optical Density | Pigeon Test |
| 5. Mrs. Lec. (age 44) depression anxious | 29 Oct'62 BO ^o =0.15 BF=0.15 BE=0.14 | 29 Oct'62 Paralyses, then death of animal 5 hrs later | 29 Oct'62 BO ^o =0.17 BF=0.17 BE=0.18 | 29 Oct'62 No paralysis normal slight trouble in flying |
| ----- | | | | |
| 6. Miss Douc. (age 33) depression, encephalopathy | 12 Nov'62 BF=0.20 | 12 Nov'62 Violent death after generalized convulsions in 2 animals | 12 Nov'62 BF=0.20 | 12 Nov'62 Aggressive- ness, then normal |
| ----- | | | | |
| 7. Miss Memer (age 45) periodic | 2 Nov'62 BF=0.16 | 22 Nov'62 Normal | | 22 Nov'62 Normal |
| ----- | | | | |
| 8. Mrs. Mor. (age 41) depression | 2 Dec'62 BO ^o =0.20 BF=0.20 BE=0.25 | 2 Dec'62 3 hrs later, sleepiness, slight torpor | 2 Dec'62 0.59 | 2 Dec'62 Slight cata- lepsy, Prehen- sion tests++ Precipitation tests++ |

| After Lyophilization | | | |
|----------------------|--|----------------|---|
| <u>Bile A</u> | | <u>Bile B</u> | |
| <u>Optical</u> | <u>Pigeon</u> | <u>Optical</u> | <u>Pigeon</u> |
| <u>Density</u> | <u>Test</u> | <u>Density</u> | <u>Test</u> |
| 5. 31 Oct.'62 | 31 Oct'62 | | |
| 0.06 | Normal state | 0.16 | Normal |
| ----- | | | |
| 6. 18 Nov'62 | 18 Nov '62 | | |
| 0.23 | Slight loss of initiative | 0.12 | Slight torpor |
| ----- | | | |
| 7. 2 Dec '62 | 2 Dec '62 | 2 Dec '62 | 2 Dec '62 |
| 0.13 | Normal Died 24 hours later | 0.20 | Torpor, then died 24 hours later |
| ----- | | | |
| 8. 6 Dec '62 | 6 Dec '62 | 6 Dec '62 | 6 Dec '62 |
| 0.18 | Slight sleepiness 3 hrs later; No catalepsy | 0.06 | Normal |

- END -